REMARKS/ARGUMENTS

Claims 1-6 and 9-10 are pending in the present application. Applicants note with appreciation that a number of prior art rejections have been withdrawn in view of the last response. The outstanding rejections are addressed below.

Status of the Claims

Claims 1-4 are amended with this response. Claim 1 has been amended to clarify that a glucosaminyl-acylphosphatidylinositol (GlcN-(acyl)PI) precursor is added to the mixture of the test sample. Support for this amendment is found, for example, at page 6, line 13 to page 7, line 2 and at page 9, line 22 to page 10, line 14 of the specification. Claim 2(c) has been amended to explicitly recite stringent hybridization conditions. Support for the amendment is found, for example, at page 2, line 32 to page 3, line 5. Claim 2(d) has also been amended to specify the number of amino acids that can be altered in the recited protein sequences. Support for this amendment is found, for example, at page 3, lines 12-13. Support for the addition of claim 2(e) is found, for example, at page 3, lines 16-19. Support for the amendments to claims 3 and 4 is found, for example, at page 1, line 13.

Seuence Listing

The Examiner has objected to the Sequence Listing submitted on July 14, 2006. A corrected Sequence Listing is filed herewith.

Applicants submit herewith a substitute Sequence Listing in paper and computer readable forms (diskette) in compliance with the provisions for patent Application Disclosures Containing Nucleotide and/or Amino Acid Sequences, 37 C.F.R. §§ 1.821-1.825.

The Sequence Listing information recorded in the computer readable form is identical to the written copy of the Sequence Listing. The Sequence Listing does not include new matter or matter that goes beyond the disclosure of the application, as filed.

Objections to the Specification

The specification was objected to because the first use of the abbreviations "GlcN-(acyl)PI", "GPI", and "GPI-anchored" does not provide the full name of these compounds. The specification has been amended, a suggested by the Examiner. The embedded hyperlink noted by the Examiner has been removed with this amendment. Finally, the specification has been amended to include generic descriptions of the trademarked products noted by the Examiner.

Double Patenting rejection

The Examiner rejects claims 1-2 and 9-10 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 7,541,332. The '332 patent granted from US Application No. 10/536,935, which was the basis for a double patenting rejection, now withdrawn.[1] The Examiner asserts that the claims of US Patent No. 7,541,332 are a species within the genus defined by claims 1-2 and 9-10. Applicants respectfully traverse this rejection.

Applicants respectfully disagree with the Examiner's characterizations of the claims of the '332 patent. At the top of page 5 of the Office Action, the Examiner characterizes these claims as reciting, *inter alia* "(2) detecting GlcN-(acyl)PI and (3) selecting the test compound that decreases GlcN-(acyl)PI." In fact, claims 1-2 of the '332 patent include the following steps "(b) detecting the binding activity between the protein and the test compound" and "(c) selecting the test compound as the compound having antifungal action if the test compound has an activity of binding to the protein" (see claim 1) or "(b) detecting the amount of transport of a glycosylphosphatidylinositol (GPI) anchored protein to the cell wall in the fungus" and "(c) selecting the test compound as the compound having an antifungal action if the test compound diminishes the amount of transport of the GPI -anchored protein to the cell wall detected in step (b) as compared to the amount of transport detected when the test sample was

[1] Applicants understand that the rejection over the claims of the '935 application is withdrawn in view of the issuance of the '332 patent. Otherwise, the maintenance of this rejection would be inconsistent in view of the withdrawal of the rejection over the claims of the '935 application.

contacted with a fungus that is not overexpressing the protein" (see claim 2). Thus, none of the claims of the '332 patent explicitly refer to GlcN-(acyl)PI as suggested by the Examiner.

Moreover, as is clear from the above, the '332 patent claims are patentably distinct from the pending claims. As discussed in the response to the previous Office Action, the '332 patent claims are directed to methods of screening which involves either the detection of binding between the GWTl protein and a candidate compound, or detection of a decreasing amount of transportation of GPI -anchored proteins. In contrast, the methods of the present invention screen for antifungal activity by detecting the amount of GlcN-(acyl)PI that is synthesized by GWT1, as a result of the transfer of an acyl group to GlcN-PI in the GPI biosynthesis pathway. The '332 patent does not disclose that the GWT1 enzyme has this activity. Thus, claims 1-2 and 9-10 are patentably distinct from claims 1-3 of the '332 patent and the obviousness-type double patenting rejection should be withdrawn.

Claim Rejections - 35 USC § 112, first paragraph

The Examiner rejects claims 1-6 and 9-10 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement and enablement requirement. The Examiner asserts that Applicants have not demonstrated that any GWT1 gene, other than the *Saccharomyces cerevisiae* gene, can be used to identify test samples that decrease GlcN-(acyl)PI and therefore have antifungal activity. Also, the Examiner asserts that the specification does not teach any functional analogues of the exemplified protein.

As an initial matter, Applicants note that the Examiner has apparently misunderstood the function of GWT1. For example at page 6, lines 25-27 of the Office Action, the Examiners states that "[t]he specification is only limited the S. Cerevisiae GWTI gene comprising the nucleotide sequence of SEQ ID NO: 1 ***capable of decreasing*** GlcN-(acyl)PI" (emphasis added). In fact, as discussed above, the function of GWT1 is to catalyze the transacylation of GPI, thus forming GlcN-(acyl)PI. Activity of the enzyme therefore leads to increased levels of GlcN-(acyl)PI, not decreased levels.

While not necessarily agreeing with the Examiner's assertions, the Applicants have amended claim 2 to further specify the claimed proteins. Specifically, stringent conditions have been defined in claim 2(c) and the number of amino acid residues which have been added, deleted, substituted, and/or inserted has been specified in claim 2(d). Furthermore, a DNA has been added in claim 2(e), encoding a protein which has more than 60% identity to the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, or 14. As explained in detail below, the DNAs of amended claim 2(c), (d) and (e) would be expected to encode proteins having the same function of the original GWT1 as set forth SEQ ID NOs: 2,4,6,8, 10, or 14 as explained below.

Applicants provide herewith two references published after filing date of the present application. The first reference, Umemura, *et al* (*J. Biol. Chem.* 278:23639-23647 (2003), Appendix A) teaches that GWT1 of *Schizosaccharomyces pombe* and *Cryptococcus neoformans* catalyze the transacylation of GPI (see page 23664, lines 16-23 of right column). In addition, pair-wise alignments between the amino acid sequences of GWT1 of *Saccharomyces cerevisiae* ("EI-A0209P-2", SEQ ID NO: 2), *Schizosaccharomyces pombe* ("EI-A0209P-8", SEQ ID NO: 8) and *Cryptococcus neoformans* ("E1-A0209P-14", SEQ ID NO: 14) are shown in the attached Appendix B. These alignments show that the identity between these three amino acid sequences is at least about 30%. Thus, one of skill would recognize that a protein comprising an amino acid sequence having as little as about 30% identity to one of these three amino acid sequences would also catalyze the transacylation of GPI.

The second reference, Murakami, *et al* (Mol. Biol. Cell 14:4285-4295 (2003), Appendix C) teaches that a rat enzyme identified as PIG-W (GWT1) catalyzes the transacylation of GPI (see "*PIG-W Is Most Likely the Acyltransferase*" at page 4289, right column). In addition, alignment results between the amino acid sequences of GWT1 of *Saccharomyces cerevisiae* and rat PIG- W (Genbank accession no. BAC77020) are shown in the attached Appendix D. The results indicate that the identity between these two amino acid sequences is also about 30%. This information provides further evidence to show that a protein comprising a amino acid sequence as little as about 30% identical to one of these two amino acid sequences catalyzes the transacylation of GPI.

The proteins encoded by the DNAs of amended claim 2(d) and (e) comprise a amino acid sequence having more than 60% identity to these three amino acid sequences, and thus it would be recognized that the claim is directed to proteins that catalyze the transacylation of GPI. Also, since stringent conditions have been defined in claim 2(c), DNAs encoding a protein having less than 30% identity to these three amino acid sequences would not be encompassed in the DNA of amended claim 2(c).

Moreover, the specification provides clear instructions and actual examples of methods for testing transacylation of GPI (*see* 2. Methods for determining transacylation activity, beginning on page 6 of the present application). Thus, variants can be readily tested for this activity.

Accordingly, in view of the evidence provided here, one of skill would recognize that GWTl variants as defined by amended claim 2 will catalyze transacylation of GPI and would thus be useful in the claimed methods.

The Examiner also questions whether there is a correlation between compounds identified by the claimed methods and antifungal activity. However, US 2004/0038239 (Appendix E) corresponding to US Application No. 10/332,340 discloses that compounds identified by the claimed methods (for example 1-(4-butylbenzyl) isoquinoline, which is described on pages 10-11 of the present application) have antifungal activity and inhibit the growth of *Saccharomyces cerevisiae* and *Candida albicans*. Thus, compounds identified by the claimed methods clearly correlate with the antifungal activity.

Rejections under 35 U.S.C. § 112, second paragraph

The Examiner rejects claims 1-6 and 9-10 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner asserts that the phrase "detecting GlcN-(acyl)PI" in claim 1 is vague and indefinite.

While not necessarily agreeing with the Examiner's assertions, the Applicants have amended claim 1 to add new step (2) "adding glucosaminyl-acylphosphatidylinositol

(GlcN-(acyl)PI) precursor to the mixture of the test sample and the protein" in order to clarify that GlcN-(acyl)PI is formed from GlcN-(acyl)PI precursor. As discussed above and as at page 10 lines 7-8 in the specification, GWT1 is an enzyme that catalyzes the formation of GlcN-(acyl)PI.

The also Examiner rejects claims 1-6 and 9-10 under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. The Examiner asserts that the performance of claimed method steps 1), 2) and 3) do not correlate to the outcome as claimed, and therefore, said method steps do not lead to stated method goal.

While not necessarily agreeing with the Examiner's assertions, the Applicants have amended claim 1 to be drawn to a method of screening for a "sample" having an antifungal activity so that the outcome of the formal step is consistent with claimed method goal. Applicants respectfully request withdrawal of the rejection.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at 415-576-0200.

Respectfully submitted,

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